Transplantasi freeze-dried membran amnion manusia pada penyembuhan ulkus kornea bakteri tinjauan ekspresi mRNA dan protein TNF-, MMP-9, TGF-1 dan TGF-2 di air mata dan jaringan kornea = Human freeze-dried amniotic membrane transplantation in bacterial corneal ulcer healing: evaluation of TNF-, MMP-9, TGF-1 and TGF-2 mRNA expression and protein in tears and corneal tissue

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Abstrak

Latar belakang: Ulkus kornea adalah salah satu penyakit infeksi mata yang banyak ditemukan di negara berkembang termasuk Indonesia. Tatalaksana ulkus kornea bakteri konvensional umumnya dapat menimbulkan jaringan parut kornea permanen yang dapat menurunkan tajam penglihatan. Penggunaan transplantasi membran amnion (TMA) pada ulkus kornea dapat mempercepat proses penyembuhan dan mengurangi terbentuknya jaringan parut kornea. Membran amnion diduga menjadi kerangka baru dan mengekspresi beberapa komponen biologis yang berperan membantu proses epitelisasi dan pembentukan jaringan parut di kornea.
Tujuan: Mengetahui dan membuktikan perbedaan perubahan klinis pada kelompok TMA dan terapi standar (non-MA) pada pasien dengan ulkus kornea bakteri, perbedaan perubahan kadar protein TNF-, MMP-9, TGF-1 di air mata dan ekspresi mRNA TNF-, MMP-9, TGF-1, dan TGF-2 di air mata dan kornea.
Metode: Penelitian tahap pertama, dilakukan penilaian klinis sebelum dan sesudah pada grup TMA dan terapi standar (non-TMA) dengan menilai tajam penglihatan, waktu epitelisasi total, waktu pembentukan sikatrik total dan derajat sikatrik serta uji kadar protein TNF-, MMP-9, TGF-1 di air mata dengan pemeriksaan ELISA. Penelitian tahap kedua, dilakukan pemeriksaan ekspresi mRNA TNF-, MMP-9, TGF-1, dan TGF-2 di air mata dan kornea dengan pemeriksaan quantitative Reverse Transcriptase-Polymerase Chain Reaction (qRT-PCR).
Hasil: Hasil penelitian pertama, pada grup TMA terjadi perbaikan yang signifikan bermakna pada tajam penglihatan (p=0.001), waktu epitelisasi total (p=0.002), waktu terbentuk sikatrik total (p=0.005), dan derajat sikatrik (p=0.001) dibandingkan grup non-TMA. Hasil kadar proteinTNF-, MMP-9, dan TGF-1 di air mata tidak terjadi perubahan yang bermakna sebelum dan sesudah dan tidak terdapat perbedaan bermakna pada kedua grup (p>0.005). Pada hasil penelitian kedua, ekspresi mRNA TNF- menurun paling tinggi pada grup TMA (0.824 ± 0), MMP-9 meningkat paling tinggi pada grup TMA (66.698 ± 24.948), TGF-1 meningkat paling tinggi pada grup TMA (34.425 ± 14.025), sedangkan TGF-2 mengalami peningkatan tertinggi pada grup non-TMA (114.049 ± 55.344).
Kesimpulan: Terdapat perbaikan klinis yang signifikan pasca TMA, sejalan dengan ekspresi gen dari molekul yang terkait ditandai dengan penurunan inflamasi, re-epitelisasi yang lebih cepat, dan pengurangan pembentukan sikatrik. Kadar protein dan ekspresi gen molekul inflamasi di air mata tidak dapat dijadikan penanda untuk proses yang terjadi di kornea.
<hr><i>Background: Corneal ulcer is one of ocular infection disease that is commonly found in developing country like Indonesia. The conventional treatment for bacterial corneal ulcer usually causes the forming of permanent corneal scar which results in decrease of visual acuity. The use of amniotic membrane

transplantation (AMT) in corneal ulcer is believed can shorten the healing process and reduce corneal scar. Amniotic membrane is expected to become as a new scaffold and have several biological properties that play a role in epithelization process and fibrotic tissue formation.
Objective: To evaluate and establish the clinical differences on amniotic membrane transplantation and standard therapy of patients with bacterial corneal ulcer, and laboratory evaluation of protein level and mRNA expression changes of TNF-, MMP-9, TGF-1 and TGF-2 in tears and corneal tissue.
Method: This study was divided into two phases on two groups of AMT and standard therapy group (non-AMT). On the first phase, clinical evaluation was examined include visual acuity, total duration of epithelization, total duration of scar formation and the degree of corneal scar, along with laboratory of protein level of TNF-, MMP-9, TGF-1 in tears with ELISA. On the second phase, mRNA expression of TNF-, MMP-9, TGF-1, and TGF-2 in tears and cornea were examined with quantitative Reverse Transcriptase-Polymerase Chain Reaction (qRT-PCR).
Result: The result of first phase on TMA group showed significant improvement on visual acuity (p=0.001), total duration of epithelization (p=0.002), total duration of scar formation (p=0.005), and cicatrix degree (p=0.001) compared to non-TMA group and a non-significant result on protein level of TNF-, MMP-9, TGF-1 in tears on both groups (p>0.005).On the second phase, mRNA expression of TNF-showed the highest decrease on TMA group (0.824 ± 0), MMP-9 showed the highest increase on group TMA (66.698 ± 24.948),TGF-1 expression increased the highest on TMA group (34.425 ± 14.025), whereas TGF-2 showed the highest result on non-TMA group (114.049 ± 55.344).
Conclusion: There was significant clinical improvement observed in TMA group parallel with related molecular genetic expression, indicated decreasing of inflammation, faster re-epithelization, and less dense scar formation. Protein level and genetic molecular expression in tears are poor predictors of processes occurring in the cornea.</i>